

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>7</sup> :</b> <b>C12N 5/10, 15/62, 15/85, A61K 48/00,</b> <b>A61P 35/00 // C07K 16/28, 14/705, 16/00</b>	<b>A3</b>	<b>(11) International Publication Number:</b> <b>WO 00/23573</b> <b>(43) International Publication Date:</b> 27 April 2000 (27.04.00)
<b>(21) International Application Number:</b> PCT/US99/24484 <b>(22) International Filing Date:</b> 20 October 1999 (20.10.99) <b>(30) Priority Data:</b> 60/105,014                      20 October 1998 (20.10.98)                      US <b>(71) Applicant:</b> CITY OF HOPE [US/US]; 1500 East Duarte Road, Duarte, CA 91010-0269 (US). <b>(72) Inventors:</b> RAUBITSCHKEK, Andrew; 1691 El Molino, San Marino, CA 91108 (US). JENSEN, Michael, C.; 2305 Woodlyn Road, Pasadena, CA 91104 (US). WU, Anna, M.; 14919 Sutton Street, Sherman Oaks, CA 91403 (US). <b>(74) Agents:</b> KERR, Don, M. et al.; Rothwell, Figg, Ernst & Kurz, Suite 701 East, 555 13th Street N.W., Columbia Square, Washington, DC 20004 (US).		<b>(81) Designated States:</b> AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i>  <b>(88) Date of publication of the international search report:</b> 8 September 2000 (08.09.00)
<b>(54) Title:</b> CD20-SPECIFIC REDIRECTED T CELLS AND THEIR USE IN CELLULAR IMMUNOTHERAPY OF CD20 <sup>+</sup> MALIG- NANCIES  <b>(57) Abstract</b>  <p>Genetically engineered, CD20-specific redirected T cells expressing a cell surface protein having an extracellular domain comprising a receptor which is specific for CD20, an intracellular signaling domain, and a transmembrane domain. Use of such cells for cellular immunotherapy of CD20<sup>+</sup> malignancies and for abrogating any untoward B cell function. In one embodiment, the cell surface protein is a single chain FvFc:ζ receptor where Fv designates the V<sub>H</sub> and V<sub>L</sub> chains of a single chain monoclonal antibody to CD20 linked by peptide, Fc represents a hinge-CH<sub>2</sub>-CH<sub>3</sub> region of a human IgG<sub>1</sub>, and ζ represents the intracellular signaling domain of the zeta chain of human CD3. A method of making a redirected T cell expressing a chimeric T cell receptor by electroporation using naked DNA encoding the receptor.</p>		

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakhstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/24484

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N5/10 C12N15/62 C12N15/85 A61K48/00 A61P35/00  
//C07K16/28,C07K14/705,C07K16/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	M. JENSEN ET AL.: "CD20 is a molecular target for scFvFc:zeta receptor redirected T cells: implications for cellular immunotherapy of CD20+ malignancy." BIOLOGY OF BLOOD AND MARROW TRANSPLANTATION, vol. 4, no. 2, 1998, pages 75-83, XP000910525 Charlottesville, VA, USA the whole document --- -/--	1-34

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

17 May 2000

Date of mailing of the international search report

30/05/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Nooij, F

# INTERNATIONAL SEARCH REPORT

Inte lional Application No

PCT/US 99/24484

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	H. ABKEN ET AL.: "Can combined T-cell- and antibody-based immunotherapy outsmart tumor cells?" IMMUNOLOGY TODAY, vol. 19, no. 1, January 1998 (1998-01), pages 1-5, XP004101455 Amsterdam, The Netherlands the whole document	1-34
Y	H. HAISMA ET AL.: "Construction and characterization of a fusion protein of single-chain anti-CD20 antibody and human beta-glucuronidase for antibody-directed enzyme prodrug therapy." BLOOD, vol. 92, no. 1, 1 July 1998 (1998-07-01), pages 184-190, XP002076505 New York, NY, USA abstract	1-34
Y	WO 97 23613 A (CELLTECH THERAPEUTICS LTD.) 3 July 1997 (1997-07-03) figures 1,2A,14,15 claims page 18, line 14 - line 29 page 19, line 26 -page 20, line 5	1-34
Y	WO 94 11026 A (IDEC PHARMACEUTICALS CORPORATION) 26 May 1994 (1994-05-26) examples claims	1-34
Y	WO 98 41613 A (G. OTTEN ET AL.) 24 September 1998 (1998-09-24) examples claims	1-34
A	D. ANDERSON ET AL.: "Targeted anti-cancer therapy using rituximab, a chimaeric anti-CD20 antibody (IDEC-C2B8) in the treatment of non-Hodgkin's B-cell lymphoma." BIOCHEMICAL SOCIETY TRANSACTIONS, vol. 25, 1997, pages 705-708, XP002078838 the whole document	1-34

-/--

# INTERNATIONAL SEARCH REPORT

Int. lional Application No

PCT/US 99/24484

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>G. GROSS ET AL.: "Endowing T cells with antibody specificity using chimeric T cell receptors."  THE FASEB JOURNAL,  vol. 6, no. 15, December 1992 (1992-12),  pages 3370-3378, XP002137900  Bethesda, MD, USA  cited in the application  page 3376, left-hand column, line 17 -  line 51  figure 1</p> <p style="text-align: center;">---</p>	1-34
A	<p>US 5 359 046 A (CAPON ET AL.)  25 October 1994 (1994-10-25)  example 3  claims</p> <p style="text-align: center;">---</p>	1-34
P, X	<p>M. JENSEN ET AL.: "Specific recognition and lysis of CD20+ lymphoma cells by primary human CD8+ CTL clones genetically modified to express a CD20-specific chimeric immunoreceptor."  BLOOD,  vol. 92, no. 10, suppl. 1 (part 1 of 2),  15 November 1998 (1998-11-15), page 245a  XP000906991  New York, NY, USA  abstract # 998</p> <p style="text-align: center;">-----</p>	1-34

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/24484

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claims 17-20 and 30-34 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/24484

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9723613 A	03-07-1997	AU 1201997 A	17-07-1997
		CA 2238873 A	03-07-1997
		EP 0870019 A	14-10-1998
		JP 2000502562 T	07-03-2000
WO 9411026 A	26-05-1994	US 5736137 A	07-04-1998
		AT 139900 T	15-07-1996
		AU 688743 B	19-03-1998
		BG 62386 B	29-10-1999
		BG 99701 A	29-02-1996
		CA 2149329 A	26-05-1994
		DE 69303494 D	08-08-1996
		DE 69303494 T	16-01-1997
		DK 669836 T	14-10-1996
		EP 0669836 A	06-09-1995
		EP 0752248 A	08-01-1997
		ES 2091684 T	01-11-1996
		FI 952327 A	10-07-1995
		GR 3020731 T	30-11-1996
		JP 8503468 T	16-04-1996
		LV 11732 A	20-04-1997
		LV 11732 B	20-10-1997
		MD 1367 B	31-12-1999
		NO 951903 A	13-07-1995
		NZ 258392 A	22-09-1997
		PL 309002 A	18-09-1995
		PL 174721 B	30-09-1998
		US 5776456 A	07-07-1998
		US 5843439 A	01-12-1998
		AU 5603294 A	08-06-1994
		CN 1094965 A	16-11-1994
		HU 72914 A	28-06-1996
		PL 175557 B	29-01-1999
		SG 45294 A	16-01-1998
		ZA 9308466 A	20-06-1994
WO 9841613 A	24-09-1998	AU 6537798 A	12-10-1998
US 5359046 A	25-10-1994	AT 145428 T	15-12-1996
		AU 643109 B	04-11-1993
		AU 9172291 A	08-07-1992
		CA 2074825 A	15-06-1992
		DE 69123241 D	02-01-1997
		DE 69123241 T	17-04-1997
		DK 517895 T	07-04-1997
		EP 0517895 A	16-12-1992
		EP 0732402 A	18-09-1996
		ES 2096749 T	16-03-1997
		GR 3022538 T	31-05-1997
		NO 923171 A	28-09-1992
		WO 9210591 A	25-06-1992

**THIS PAGE BLANK (USPTO)**